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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/623,914 | 07/21/2003 | Thomas M. Hering | 27708/03905 | 5367 |

24024 7590 10/18/2006

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| EXAMINER | |
|---|---|
| DUNSTON, JENNIFER ANN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1636 | |

DATE MAILED: 10/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/623,914 | HERING ET AL. | |
| | Examiner | Art Unit | |
| | Jennifer Dunston | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *8-34* is/are pending in the application.

4a) Of the above claim(s) *15-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 July 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/24/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Exhibits A and B*.

## DETAILED ACTION

Receipt is acknowledged of an amendment, filed 7/21/2003, in which claims 1-7 were canceled. Currently, claims 8-34 are pending.

### *Election/Restrictions*

Applicant's election without traverse of Group I (claims 8-14) in the reply filed on 8/11/2006 is acknowledged.

Claims 15-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/11/2006.

An examination on the merits of claims 8-14 follows.

### *Sequence Compliance*

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below.

Paragraphs [0047], [0048] and [0102] contain amino acid sequences that are not referred to by the use of a sequence identifier (for example, the HTGEKP linker sequence and zinc finger motif sequence of paragraph [0047]). Where the description or claims of a patent application discuss a sequence that is set forth in the Sequence Listing, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the

description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Further, the specification indicates that the sequence presented in Figure 6 is disclosed in SEQ ID NO: 4 and is encoded by SEQ ID NO: 3 (e.g. paragraphs [0031 and [0056]). However, the sequence of SEQ ID NO: 4 is not identical to the sequence disclosed in Figure 6 and is not identical to the sequence encoded by SEQ ID NO: 3 (see the attached alignment in Exhibit B).

In response to this office action, Applicant must comply with the sequence rules, 37 CFR 1.821 - 1.825. The nature of the non-compliance did not preclude an examination of the elected invention on the merits, the results of which are presented below.

### *Information Disclosure Statement*

Receipt of an information disclosure statement, filed on 10/24/2003, is acknowledged. The signed and initialed PTO 1449 has been mailed with this action.

### *Drawings*

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: parts A-D of Figure 3 and parts A-C of Figure 5 are not separately described. The parts of the figure appear to be continuations of the sequences described in the specification within the brief description of the drawings. It would be remedial to remove the reference letters within the drawings for Figures 3 and 5. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37

CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

It is noted that a color photograph or drawing was submitted for Figure 11. Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2). If Applicant does not wish to submit a petition, Figure 11 will be depicted as a black and white figure.

### *Specification*

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See paragraph [0105].

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8-13 are drawn to polynucleotides that encode CZF-2 protein variants of SEQ ID NO: 4. The specification indicates that the sequence presented in Figure 6 is disclosed in SEQ ID NO: 4 and is encoded by SEQ ID NO: 3 (e.g. paragraphs [0031 and [0056]). However, the sequence of SEQ ID NO: 4 is not identical to the sequence disclosed in Figure 6 and is not identical to the sequence encoded by SEQ ID NO: 3 (see the attached alignment in Exhibit B). The metes and bounds of the claims are unclear, because it is unclear if the claims are referring to the sequence disclosed in the figure as SEQ ID NO: 4 or the sequence disclosed in the sequence listing as SEQ ID NO: 4.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-12 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 8-12 are drawn to an isolated polynucleotide comprising a coding sequence for a CZF-2 protein or a variant thereof. Claim 8 limits the protein variant to an amino acid sequence at least 90% identical to SEQ ID NO: 4. Claim 9 limits the protein variant to a sequence which is at least 95% identical to SEQ ID NO: 4. Claim 11 further limits the protein variant of claim 9 to one that is immunoreactive with an antibody produced by immunizing an animal with a protein comprising the sequence of SEQ ID NO: 4. Claim 10 limits the protein variant to a sequence which is at least 97% identical to SEQ ID NO: 4. Claim 12 limits the polynucleotide of claim 8 to one that comprises a sequence which hybridizes under highly stringent conditions to SEQ ID NO: 3. Claims 8, 9 and 10 recite the phrase "an amino acid sequence" in reference to SEQ ID NO: 4. Thus, the claims encompass polynucleotides that encode the full length sequence of SEQ ID NO: 4, sequences that are 90%, 95% or 97% identical to the full length sequence of SEQ ID NO: 4, and dipeptides or oligopeptides of SEQ ID NO: 4. The term "an amino acid sequence" reads on sequences of two or more amino acids found within SEQ ID NO: 4. Claim 12 recites the phrase "a sequence which hybridizes under highly stringent conditions to SEQ ID NO: 3." The specification defines the term "highly stringent conditions" as an overnight

incubation at 42 °C in a solution comprising 50% formamide, 5x SSC, 50 mM sodium phosphate (ph7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 μg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.2 x SSC at about 65 °C (paragraph [0059]). Thus, claim 12 encompasses any sequence capable of hybridizing to SEQ ID NO: 3 under the abovementioned conditions, including fragments and variants of SEQ ID NO: 3, that encode at least two amino acids (i.e. an amino acid sequence) of SEQ ID NO: 4.

Claim 14 is drawn to an isolated polynucleotide selected from the group consisting of (a) an isolated polynucleotide comprising a sequence which hybridizes under highly stringent conditions to a sequence comprising, consecutively, nucleotide 25 through nucleotide 1581 of SEQ ID NO: 3; (b) an isolated polynucleotide comprising a sequence which is complementary to a sequence which hybridizes under highly stringent conditions to a sequence comprising, consecutively, nucleotide 25 through nucleotide 1581 of SEQ ID NO: 3; (c) an isolated polynucleotide comprising a sequence which hybridizes under highly stringent conditions to a sequence comprising, consecutively, nucleotide 163 through nucleotide 423 of SEQ ID NO: 3; and (d) an isolated polynucleotide comprising a sequence which is complementary to a sequence which hybridizes under highly stringent conditions to a sequence comprising, consecutively, nucleotide 163 through nucleotide 423 of SEQ ID NO: 3. The specification defines the term "highly stringent conditions" as an overnight incubation at 42 °C in a solution comprising 50% formamide, 5x SSC, 50 mM sodium phosphate (ph7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 μg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.2 x SSC at about 65 °C (paragraph [0059]). Thus, the claim encompasses any fragment or

variant of SEQ ID NO: 3 within the specified nucleotides that hybridizes under highly stringent conditions, or the complement thereof.

The rejected claims thus comprise a genus of polynucleotides that encompass polynucleotides that encode fragments and variants of SEQ ID NO: 4 and fragments and variants of SEQ ID NO: 3. The specification defines the term "variant" as a protein whose amino acid sequence is similar to one of the amino acid sequences shown in Figs. 4 and 6, but does not have 100% identity to the reference sequence. Thus, the claimed polynucleotides encode proteins with any combination of deletions, substitutions or insertions to result in "a sequence" that is at least 90% identical to SEQ ID NO: 4. Accordingly, the claims encompass a large genus of polynucleotides.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification describes CZF-2 as a 2166 bp sequence containing a 518 amino acid open reading frame, containing a KRAB-A domain and 12 zinc-finger domains (e.g. Figure 6). SEQ ID NO: 3 is nucleic acid sequence of 2143 nucleotides that encodes the 518 amino acid protein of SEQ ID NO: 4. The specification envisions using CZF-2 polynucleotides and fragments to detect and stage chondrogenesis in cells (e.g. paragraphs [0022] and [0063]). The specification envisions making antibodies from peptides comprising at least 10 amino acids of the sequence of SEQ ID NO: 4 (e.g. paragraph [0095]). The specification does not describe fragments and variants of SEQ ID NO: 4 that would result in the production of antibodies that

can be used to detect and stage chondrogenesis. The specification does not describe the common structural attributes necessary for the detection and staging of chondrogenesis for peptides other than SEQ ID NO: 4 or nucleic acid sequences other than SEQ ID NO: 3.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Given the very large genus of polynucleotides encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to the necessary shared structure for variants, the skilled artisan would not have been able to envision a

sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus of polynucleotides. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention for claims 8-12 and 14.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 8-10, 12 and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Brennan et al (US 5,985,551; see the entire reference).

Brennan et al teach an oligonucleotide array plate comprising every possible 10-mer oligonucleotide having 10 nucleotides (e.g. column 9, lines 9-43).

The rejected claims read on the teachings of Brennan et al, because Brennan teach every possible nucleic acid sequence of 10 nucleotides. Thus, Brennan et al necessarily teach ten nucleotides that encode three amino acids that are 100% identical to SEQ ID NO: 4. Further, Brennan et al necessarily teach a 10-mer that will hybridize under highly stringent conditions to a sequence with nucleotide 25-1581 and 163-423, and complements thereof, of SEQ ID NO: 3.

Claims 8-12 and 14 are rejected under 35 U.S.C. 102(a) as being anticipated by GenBank Accession No. AC011508.1 (GI: 6015244, October 7, 1999; see the entire reference).

GenBank Accession No. AC011508 teaches a polynucleotide with a sequence 100% identical to a sequence within nucleotides 25-1581 and nucleotides 163-423 of instant SEQ ID NO: 3 (see the alignment in Exhibit A).

The rejected claims read on the teachings of GenBank Accession No. AC011508.1, because the nucleotide sequence disclosed encodes an amino acid sequence with 100% identity to an amino acid sequence (i.e. two or more amino acids) of SEQ ID NO: 4. This portion of the protein would inherently bind to an antibody raised against this portion of SEQ ID NO: 4, because they would have the same sequence, which could be recognized by an antibody raised against the peptide sequence. Furthermore, the nucleotide sequence disclosed in GenBank Accession No. AC011508 would hybridize under highly stringent conditions to a sequence within nucleotides 25-1581 and 163-423 of SEQ ID NO: 3.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

jad

CELINE QIAN, PH.D.
PRIMARY EXAMINER

# Blast 2 Sequences results

PubMed Entrez BLAST OMIM Taxonomy Structure

**BLAST 2 SEQUENCES RESULTS VERSION BLASTN 2.2.14 [May-07-2006]**

Match: 1 Mismatch: -2 gap open: 5 gap extension: 2
x_dropoff: 50 expect: 10.000 wordsize: 11 Filter ☑ View option Standard
Masking character option X for protein, n for nucleotide Masking color option Black
☐ Show CDS translation Align

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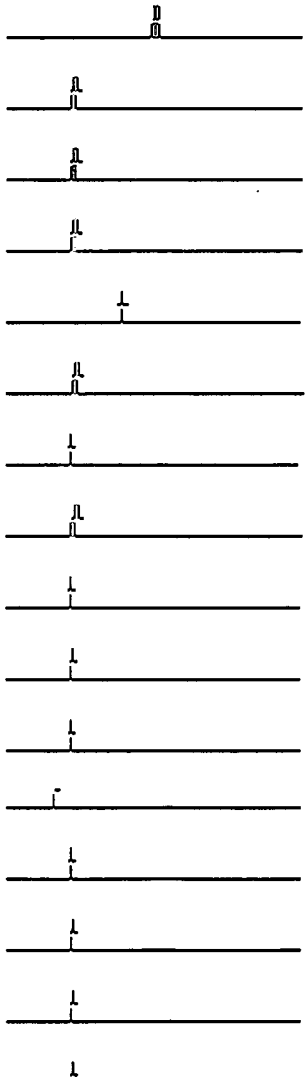
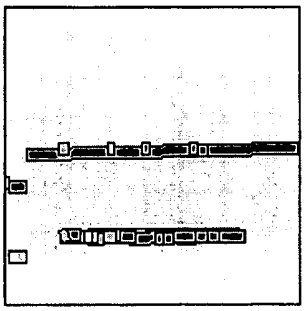
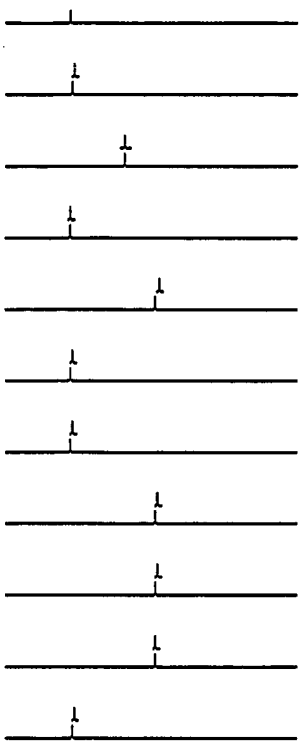
**Sequence 1**: lcl|seq_1
Length = 2143 (1 .. 2143)

**Sequence 2**: gi|6015244|gb|AC011508.1|AC011508
Length = 104342 (1 .. 104342)





1

NOTE:Bitscore and expect value are calculated based on the size of the nr database.

NOTE:If protein translation is reversed, please repeat the search with reverse strand of the query sequence.

```
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 Identities = 1951/1958 (99%), Gaps = 1/1958 (0%)
 Strand=Plus/Plus

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Query  220    ATAAATTTTTCCCAGTGGGAGATGAAGGACAAAAGTAAAACCCTTGGCCTTGAGGCATCC  279
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Query  280    ATCTTCAGAAATAATTGGAAGTGCAAAAGCATATTCGAGGGACTAAAAGGACATCAAGAG  339
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Query  400    TCTCTTACTCCACATCAAAGAATTCATAATACAGAGAAATCCTATGTTTGTAAGGAATGT  459
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Query  520    AAGCACTTTGAATGTAAAGAATGTGGGAAGAATTATTTAAGTGCCTATCAACTCAATGTG  579
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Query  580    CATCAGAGATTTCATACTGGTGAGAAACCCTATGAGTGTAAGGAATGTGGGAAGACCTTT  639
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Query  760    CATATTGGTGTGAAATCTTATAAATGTAAGGAATGTGGGAAGGCCnnnnnnnGGGGCTCA  819
              |||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Query  820    AGCCTTGCTAAACATGAGATAATTCATACAGGTGAGAAACCTTATAAATGTAAAGAATGT  879
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Query  880    GGGAAGGCCTTCAGTCGTGGCTATCAACTTACTCAGCATCAGAAAATCCATACTGGTAAG  939
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Query  940    AAACCTTATGAATGTAAAATATGTGGAAAGGCTTTTTGTTGGGGCTATCAACTTACTCGA  999
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Sbjct  53135  AAACCTTATGAATGTAAAATATGTGGAAAGGCTTTTTGTTGGGGCTATCAACTTACTCGA  53194

Query  1000   CATCAGATATTTCATACTGGTGAGAAACCCTATGAATGCAAGGAATGTGGGAAGGCTTTT  1059
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Sbjct  53195  CATCAGATATTTCATACTGGTGAGAAACCCTATGAATGCAAGGAATGTGGGAAGGCTTTT  53254

Query  1060   AATTGCGGATCAAGTCTTATTCAACATGAAAGAATTCATACTGGTGAGAAACCTTATGAA  1119
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Sbjct  53255  AATTGCGGATCAAGTCTTATTCAACATGAAAGAATTCATACTGGTGAGAAACCTTATGAA  53314

Query  1120   TGTAAAGAATGTGGAAAGGCCTTTAGTCGTGGCTATCACCTTTCTCAACATCAGAAAATC  1179
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Query  1180   CATACTGGTGAGAAACCTTTTGAATGTAAGGAATGTGGGAAGGCCTTTAGTTGGGGTTCA  1239
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  53375  CATACTGGTGAGAAACCTTTTGAATGTAAGGAATGTGGGAAGGCCTTTAGTTGGGGTTCA  53434

Query  1240   AGCCTTGTTAAACATGAGAGAGTTCATACTGGTGAGAAATCCCATGAATGTAAAGAATGC  1299
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  53435  AGCCTTGTTAAACATGAGAGAGTTCATACTGGTGAGAAATCCCATGAATGTAAAGAATGC  53494

Query  1300   GGAAAGACCTTTTGTAGTGGGTATCAACTTACTCGACATCAGGTATTTCACACTGGTGAG  1359
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Query  1360   AAACCCTATGAATGTAAGGAATGTGGGAAGGCTTTTAATTGTGGATCAAGCCTTGTTCAA  1419
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Sbjct  53555  AAACCCTATGAATGTAAGGAATGTGGGAAGGCTTTTAATTGTGGATCAAGCCTTGTTCAA  53614

Query  1420   CATGAAAGAATCCATACAGGGGAGAAACCCTATGAATGTAAAGAATGT-GGAAGGCTTTT  1478
              |||||||||||||||||||||||||||||||||||||||||||||| ||||||||||||
Sbjct  53615  CATGAAAGAATCCATACAGGGGAGAAACCCTATGAATGTAAAGAATGTGGGAAGGCTTTT  53674

Query  1479   AGTCGTGGCTATCACCTTACTCAACATCAGAAAATTCATACCGGTGAGAAACCTTTCAAA  1538
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Sbjct  53675  AGTCGTGGCTATCACCTTACTCAACATCAGAAAATTCATACCGGTGAGAAACCTTTCAAA  53734

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Sbjct  53735  TGTAAGGAATGTGGGAAGGCCTTCAGTTGGGGTTCAAGCCTAGTTAAGCATGAGAGAGTC  53794

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Sbjct  53795  CATACTAATGAGAAGTCTTATGAATGTAAAGACTGTGGGAAGGCCTTTGGTAGTGGCTAT  53854

Query  1659   CAACTTAGTGTTCATCAGAGATTTCATACTGGTGAGAAGCTTTATCAACATAAGGAATTC  1718
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Sbjct  53855  CAACTTAGTGTTCATCAGAGATTTCATACTGGTGAGAAGCTTTATCAACGTAAGGAATTC  53914

Query  1719   GGGAAGACCTTTACTCGTGGCTCAAAACTTGTTCATGAGAGAACTCATAGTAATGATAAA  1778
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Sbjct  53915  GGGAAGACCTTTACTTGTGGCTCAAAACTTGTTCATGAGAGAACTCATAGTAATGATAAA  53974

Query  1779   CCCTACAAATATAACGAATGTGGGGAAGCCTTTCTGTGGACAACTTACTCAAATGAGAAA  1838
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Query  1899   AGACAACTTATCATAATAAGAACTCTTACTCTTGAGAAACCTTGTGAATGTAAGGGTTGT  1958
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  54095  AGACAACTTATCATAATAAGAACTCTTACTCTTGAGAAACCTTGTGAATGTAAGGGTTGT  54154

Query  1959   GCAAAAGCCATTCATTTCTGTTTATGGGCAATTATCTTGCTATCCAGCAATTCATACTAG  2018
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Query  2019   TGAGAAATATTTTGAATATAATTAATATGAAAAGGCCTTTAGACTTCTGTACAGTCTTAT  2078
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  54215  TGAGAAATATTTTGAATATAATTAATATGAAAAGGCCTTTAGACTTCTGTACAGTCTTAT  54274

Query  2079   TGGATATCAATTTATACTGATGTAAAATCATTTAAATG  2116
              |||||||||||||||||||||||||||||||||||||
Sbjct  54275  TGGATATCAATTTATACTGATGTAAAATCATTTAAATG  54312
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Exhibit B

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RESULT 1
AR360880
LOCUS       AR360880                2143 bp    DNA     linear   PAT 17-AUG-2003
DEFINITION  Sequence 3 from patent US 6596855.
ACCESSION   AR360880
VERSION     AR360880.1  GI:33768379
KEYWORDS    .
SOURCE      Unknown.
  ORGANISM  Unknown.
            Unclassified.
REFERENCE   1  (bases 1 to 2143)
  AUTHORS   Hering,T.M. and Johnstone,B.
  TITLE     Probes for chondrogenesis
  JOURNAL   Patent: US 6596855-A 3 22-JUL-2003;
            Case Western Reserve University; Cleveland, OH;
            WOX;
FEATURES             Location/Qualifiers
     source          1. .2143
                     /organism="unknown"
                     /mol_type="genomic DNA"
ORIGIN

Alignment Scores:
Pred. No.:              6e-260          Length:         2143
Score:                  2861.00         Matches:        514
Percent Similarity:     99.2%           Conservative:   0
Best Local Similarity:  99.2%           Mismatches:     4
Query Match:            99.0%           Indels:         0
DB:                     2               Gaps:           0

US-10-623-914-4 (1-518) x AR360880 (1-2143)

Qy          1 MetThrAspGlyLeuValThrPheArgAspValAlaIleAspPheSerGlnGluGluTrp 20
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         25 ATGACTGATGGGTTGGTGACATTCAGGGATGTGGCCATCGACTTCTCTCAGGAGGAGTGG 84

Qy         21 GluCysLeuAspProAlaGlnArgAspLeuTyrValAspValMetLeuGluAsnTyrSer 40
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         85 GAATGCCTGGACCCTGCTCAGAGGGACTTGTACGTGGATGTAATGTTGGAGAACTATAGT 144

Qy         41 AsnLeuValSerLeuAspLeuGluSerLysThrTyrGluThrLysLysIlePheSerGlu 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        145 AACTTGGTGTCACTGGATTTGGAGTCAAAAACGTATGAGACCAAAAAAATATTTTCAGAA 204

Qy         61 AsnAspIlePheGluIleAsnPheSerGlnTrpGluMetLysAspLysSerLysThrLeu 80
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        205 AATGATATTTTTGAAATAAATTTTTCCCAGTGGGAGATGAAGGACAAAAGTAAAACCCTT 264

Qy         81 GlyLeuGluAlaSerIlePheArgAsnAsnTrpLysCysLysSerIlePheGluGlyLeu 100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        265 GGCCTTGAGGCATCCATCTTCAGAAATAATTGGAAGTGCAAAAGCATATTCGAGGGACTA 324

Qy        101 LysGlyHisGlnGluGlyTyrPheSerGlnMetIleIleSerTyrGluLysIleProSer 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        325 AAAGGACATCAAGAGGGATACTTCAGTCAAATGATAATCAGCTATGAAAAAATACCTTCT 384

Qy        121 TyrArgLysSerLysSerLeuThrProHisGlnArgIleHisAsnThrGluLysSerTyr 140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        385 TACAGAAAAAGTAAATCTCTTACTCCACATCAAAGAATTCATAATACAGAGAAATCCTAT 444

Qy        141 ValCysLysGluCysGlyLysAlaCysSerHisGlySerLysLeuValGlnHisGluArg 160
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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        445 GTTTGTAAGGAATGTGGGAAGGCTTGCAGTCATGGCTCAAAACTTGTTCAACATGAGAGA 504

Qy        161 ThrHisThrAlaGluLysHisPheGluCysLysGluCysGlyLysAsnTyrLeuSerAla 180
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        505 ACTCATACAGCTGAAAAGCACTTTGAATGTAAAGAATGTGGGAAGAATTATTTAAGTGCC 564

Qy        181 TyrGlnLeuAsnValHisGlnArgPheHisThrGlyGluLeuProTyrGluCysLysGlu 200
                ||||||||||||||||||||||||||||||||||||||||   ||||||||||||||||||
Db        565 TATCAACTCAATGTGCATCAGAGATTTCATACTGGTGAGAAACCCTATGAGTGTAAGGAA 624

Qy        201 CysGlyLysThrPheSerTrpGlySerSerLeuValLysHisGluArgIleGlyThrGly 220
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||   ||||||
Db        625 TGTGGGAAGACCTTTAGCTGGGGATCAAGCCTTGTTAAACATGAGAGAATTCACACTGGT 684

Qy        221 GluLysProTyrGluCysLysGluCysGlyLysAlaPheSerArgGlyTyrHisLeuThr 240
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        685 GAGAAACCCTATGAATGTAAAGAATGTGGGAAGGCCTTTAGTCGTGGCTATCACCTTACC 744

Qy        241 GlnHisGlnLysIleHisIleGlyValLysSerTyrLysCysLysGluCysGlyLysAla 260
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        745 CAACATCAGAAAATTCATATTGGTGTGAAATCTTATAAATGTAAGGAATGTGGGAAGGCC 804

Qy        261 PhePheTrpGlySerSerLeuAlaLysHisGluIleIleHisThrGlyGluLysProTyr 280
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        805 TTTTTTTGGGGCTCAAGCCTTGCTAAACATGAGATAATTCATACAGGTGAGAAACCTTAT 864

Qy        281 LysCysLysGluCysGlyLysAlaArgSerArgGlyTyrGlnLeuThrGlnHisGlnLeu 300
                ||||||||||||||||||||||||   ||||||||||||||||||||||||||||||
Db        865 AAATGTAAAGAATGTGGGAAGGCCTTCAGTCGTGGCTATCAACTTACTCAGCATCAGAAA 924

Qy        301 IleHisThrGlyLysLysProTyrGluCysLysIleCysGlyLysAlaPheCysTrpGly 320
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        925 ATCCATACTGGTAAGAAACCTTATGAATGTAAAATATGTGGAAAGGCTTTTTGTTGGGGC 984

Qy        321 TyrGlnLeuThrArgHisGlnIlePheHisThrGlyGluLysProTyrGluCysLysGlu 340
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Db        985 TATCAACTTACTCGACATCAGATATTTCATACTGGTGAGAAACCCTATGAATGCAAGGAA 1044

Qy        341 CysGlyLysAlaPheAsnCysGlySerSerLeuIleGlnHisGluArgIleHisThrGly 360
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1045 TGTGGGAAGGCTTTTAATTGCGGATCAAGTCTTATTCAACATGAAAGAATTCATACTGGT 1104

Qy        361 GluLysProTyrGluCysLysGluCysGlyLysAlaPheSerArgGlyTyrHisLeuSer 380
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Db       1105 GAGAAACCTTATGAATGTAAAGAATGTGGAAAGGCCTTTAGTCGTGGCTATCACCTTTCT 1164

Qy        381 GlnHisGlnLysIleHisThrGlyGluLysProPheGluCysLysGluCysGlyLysAla 400
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1165 CAACATCAGAAAATCCATACTGGTGAGAAACCTTTTGAATGTAAGGAATGTGGGAAGGCC 1224

Qy        401 PheSerTrpGlySerSerLeuValLysHisGluArgValHisThrGlyGluLysSerHis 420
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1225 TTTAGTTGGGGTTCAAGCCTTGTTAAACATGAGAGAGTTCATACTGGTGAGAAATCCCAT 1284

Qy        421 GluCysLysGluCysGlyLysThrPheCysSerGlyTyrGlnLeuThrArgHisGlnVal 440
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1285 GAATGTAAAGAATGCGGAAAGACCTTTTGTAGTGGGTATCAACTTACTCGACATCAGGTA 1344

Qy        441 PheHisThrGlyGluLysProTyrGluCysLysGluCysGlyLysAlaPheAsnCysGly 460
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db       1345 TTTCACACTGGTGAGAAACCCTATGAATGTAAGGAATGTGGGAAGGCTTTTAATTGTGGA 1404

Qy        461 SerSerLeuValGlnHisGluArgIleHisThrGlyGluLysProTyrGluCysLysGlu 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1405 TCAAGCCTTGTTCAACATGAAAGAATCCATACAGGGGAGAAACCCTATGAATGTAAAGAA 1464

Qy        481 CysGlyArgLeuLeuValValAlaIleThrLeuLeuAsnIleArgLysPheIleProVal 500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1465 TGTGGAAGGCTTTTAGTCGTGGCTATCACCTTACTCAACATCAGAAAATTCATACCGGTG 1524

Qy        501 ArgAsnLeuSerAsnValArgAsnValGlyArgProSerValGlyValGlnAla 518
              ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1525 AGAAACCTTTCAAATGTAAGGAATGTGGGAAGGCCTTCAGTTGGGGTTCAAGCC 1578
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